Atrial Fibrillation and Stroke

To the Editor:

Clinical studies of embolic stroke are inherently difficult, given the uncertainties engendered by imprecise diagnosis. The recent report of Sage and VanUitert concerning recurrent stroke in patients with nonvalvular atrial fibrillation (NVAF) emphasized that the natural history of NVAF-associated stroke may be different from embolic stroke associated with rheumatic heart disease and that a prospective study to assess the value of anticoagulation in NVAF patients is warranted.1 Several of their results with important clinical implications prompt critical comment.

The fraction of the patients that had a thrombotic rather than a cardioembolic basis for their cerebral infarction is unclear. Angiographic demonstration of carotid atherosclerotic disease identified five patients who were excluded from the study. Of the remaining 140 patients the authors state that “cerebral angiography, performed in 3 patients, demonstrated cut off distal vessels.” Did any of the other 137 patients undergo cerebral angiography? If not, the implication is that 5 of 8 (63%) patients angiogrammed had carotid atherosclerotic disease.

The evidence for emboli in 89 patients was the finding of limb emboli (18), distal cut-off on angiogram (3), peripheral lucencies on CT (14), cortical infarction at autopsy (9), or microscopic hematuria (57). We wonder about the other 51 patients: were they thought to have emboli also or cerebral atherosclerotic disease?

The Framingham data, cited by the authors, show that NVAF patients have five times the stroke risk of a matched population without this dysrhythmia.2 Unless NVAF is somehow protective for other causes of stroke, a minimum of 17% of strokes in NVAF patients are not related to NVAF. Two other studies have estimated, on the basis of imperfect clinical data, that 23–26% of strokes in NVAF patients are nonembolic.3,4 Hence, it is likely (if inevitable) that many patients in this retrospective study have nonembolic stroke. Currently available noninvasive techniques (including cardiac CT and digital subtraction angiography) may allow better definition of stroke mechanisms in future studies.

Early (within two weeks) recurrent embolism was reported to occur in only one of 59 NVAF patients. This 2% incidence has important implications for the use of immediate anticoagulation for this most common source of brain embolism. However, the early recurrence rate in an additional 53 patients (38% of the total) who succumbed during initial hospitalization was not given, nor was it known in 28 further patients without accurate follow-up.

As early recurrence of embolism predisposes to death, the early recurrence for the entire group of 140 patients is crucial. Six other clinical studies have estimated an early recurrence rate of 5–20% in NVAF-associated stroke.5–10

Finally, Sage and VanUitert conclude that the risk of recurrent emboli in NVAF remains at a relatively constant high level for at least nine years. However, their data after five years is based on follow-up of only 8 patients. Also, there were 45 “dropouts” who apparently survived but were unaccounted for at five years. Long-term follow-up may have been biased in favor of patients with further emboli, leading to hospitalization. Of 20 episodes of recurrent embolism within five years, nine (45%) occurred within one year of the initial stroke. Thus, their data, interpreted another way, suggest a particularly vulnerable period in the months following initial embolism. Although we agree that late risk of recurrent embolism is not insignificant, the magnitude of this risk is as yet unclear.6, 10

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References


Response to LETTER by Hart, Sherman, and Easton

A percentage of patients with atrial fibrillation (AF) and stroke inevitably have had a thrombotic rather than a cardioembolic basis for cerebral infarction. The key problem is trying to estimate the number of patients in each category. To support the viewpoint that a large number of our patients may have had a thrombotic stroke, Drs. Hart, Sherman and Easton have pointed out that 51 patients had no corroborating evidence for systemic emboli, and that more than half of the angiographic abnormalities showed cardiac disease. To support the opposite view, we would argue that systemic emboli, unlike cerebral emboli, often do not cause obvious deficits and may go unnoticed. Therefore, although the chance of having a non-cardiac source is greater among the 51 patients than the remainder, the observation that 89 of the entire group had evidence for systemic emboli makes an extra-cerebral basis for any given patient’s stroke likely. Also, in a group of patients with AF and stroke, physicians were inclined to angiogram only those with the greatest chance of having cardiac atherosclerotic disease. In short, no attempt to categorize patients by clinical, laboratory or radiographic criteria circumvents the possibility of estimating accurately the true percentage of thrombotic infarctions. We wish, therefore, to re-emphasize that the results are only applicable to groups of patients with the uniform presentation of stroke. AF and nonvalvular heart disease.

Of concern are differences in the timing of recurrence between our patients and others. Hart et al reported early recurrences among a total of 44 patients with AF and stroke.2 This is not significantly different (x2; p > 0.01) than 1 in 59 reported by us. The 13 patients not heparinized with nonvalvular atrial fibrillation in the cerebral embolism study group are too few in number to evaluate.3 To suggest that early recurrence is a major problem in our group because 45% of recurrent stroke in the first 5 years occurred within the first year, ignores the fact that the pool of available patients regrettably but inevitably decreases rapidly with each year of follow-up. In addition, we were unable to convince ourselves of a single recurrence among the 53 patients who worsened and died of the initial stroke. Taken together with the observation that only 1 of 59 survivors had an early recurrence, we concluded that early recurrence is not a frequently encountered problem. Moreover, we do not feel that this is an artifact associated with hospital-based retrospective analysis.

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